

Citation for published version:

Tansley, SL & McHugh, NJ 2020, 'Comment on: The reliability of immunoassays to detect autoantibodies in patients with myositis is dependent on autoantibody specificity: reply', *Rheumatology (Oxford, England)*, vol. 59, no. 8, pp. 2177-2178. <https://doi.org/10.1093/rheumatology/keaa147>

DOI:

[10.1093/rheumatology/keaa147](https://doi.org/10.1093/rheumatology/keaa147)

Publication date:

2020

Document Version

Peer reviewed version

[Link to publication](https://doi.org/10.1093/rheumatology/keaa147)

This is a pre-copyedited, author-produced version of an article accepted for publication in *Rheumatology* following peer review. The version of record Tansley, SL & McHugh, NJ 2020, 'Comment on: The reliability of immunoassays to detect autoantibodies in patients with myositis is dependent on autoantibody specificity: reply', *Rheumatology (Oxford, England)*. is available online at: <https://doi.org/10.1093/rheumatology/keaa147>

University of Bath

Alternative formats

If you require this document in an alternative format, please contact:
openaccess@bath.ac.uk

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Comment on: The reliability of immunoassays to detect autoantibodies in patients with myositis is dependent on autoantibody specificity: Reply.

Sarah L Tansley¹ and Neil J McHugh¹

1. Department of Pharmacy and Pharmacology, University of Bath, Bath, UK

Corresponding author

Dr Sarah Tansley

The University of Bath, Claverton Down, Bath, BA2 7AY

s.l.tansley@bath.ac.uk

Dear Editor,

The aim of our recent study 'The reliability of immunoassays to detect autoantibodies in patients with myositis is dependent on autoantibody specificity' was to determine the reliability of commercially available immunoassays to detect myositis specific autoantibodies (MSA) [1]. In order to investigate this a variety of statistical methods were used to assist with data interpretation. Sensitivity and specificity were calculated for each autoantibody and are shown in tables 1 and 2 [1]. As stated by Dr Sabour in the associated matters arising letter [2], these provide useful measures of the accuracy of the test. Positive and negative predictive values would not be helpful here, as these depend on the prevalence of MSA in the background population which would be expected to vary depending on which patient groups are subject to testing.

Cohens K was chosen as a measure of agreement between the commercial immunoassay being evaluated and immunoprecipitation as the gold standard test. This has been used previously in similar studies evaluating MSA testing [3-5]. Results provided by immunoprecipitation are not quantitative but simply positive or negative. Similarly, whilst the DTek blue diver assay provides a quantitative and the Euroimmun line blot semi-quantitative results there is, as yet, no known robust clinical application for MSA titres. All results were therefore categorised as positive or negative using manufacturers recommended cut-offs. Intra class correlation coefficient or Bland Altman plots suggested by Dr Sabour could not be usefully applied to this type of data. Cohens K takes into account the possibility of agreement occurring by chance and is therefore thought to be a more robust measure than simple percentage agreement calculations. We are aware that a potential limitation includes that different K values could be obtained for the same percentage agreement if one test were to give similar percentages in each category (i.e. an equal number of positives and negatives). This should not and did not occur in this study as samples were selected on the basis of their MSA status as determined by immunoprecipitation. For each MSA of interest there were 10-25 known positives and 362-460 known negatives, as shown in the results tables for each assay. For neither commercial assay evaluated was there anywhere approaching an equal number of positive and negative results for any of the MSA assessed.

We concluded that the assays analysed do not perform well for all MSA specificities and overall false positives are relatively common. Whilst this may seem a sweeping statement, our results revealed that Euroimmun line blot failed to detect any of the 14 anti-OJ samples and the DTek blue diver detected just one of these and none of the nine anti-Zo samples. Our conclusion was that this is an exceptionally poor performance for these MSA and this is an important message to clinicians. Furthermore, while the false positive rate amongst healthy controls of approximately 13% for both assays was lower than that reported by some studies[6] we would argue that this is high enough to have significant implications for widespread clinical testing and our conclusions are therefore valid.

References

1. Tansley, S., et al., *The reliability of immunoassays to detect autoantibodies in patients with myositis is dependent on autoantibody specificity*. Rheumatology, 2020. Epub ahead of print
2. Sabour, S. *Comment on: The reliability of immunoassays to detect autoantibodies in patients with myositis is dependent on autoantibody specificity*. Rheumatology...
3. Cavazzana, I., et al., *Evaluation of a novel particle-based assay for detection of autoantibodies in idiopathic inflammatory myopathies*. J Immunol Methods, 2019: p. 112661.
4. Espinosa-Ortega, F., et al., *Comparison of autoantibody specificities tested by a line blot assay and immunoprecipitation-based algorithm in patients with idiopathic inflammatory myopathies*. Ann Rheum Dis, 2019.
5. Mahler, M., et al., *Comparison of Three Immunoassays for the Detection of Myositis Specific Antibodies*. Front Immunol, 2019. **10**: p. 848.
6. Bundell, C., et al., *Diagnostic performance of a commercial immunoblot assay for myositis antibody testing*. Pathology, 2016. **48**(4): p. 363-6.

Disclosures: The authors have declared no conflicts of interest

Funding: No specific funding was received from any funding bodies in the public, commercial or not-for-profit sectors to carry out the work described in this manuscript.

Acknowledgements: The original study was supported by a grant from CureJM. S.T. is supported by funding from the Bath Institute of Rheumatic Diseases.